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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,114	01/26/2001	Michael A. Whitney	AURO1120-5	8989

7590 09/05/2003

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/772,114	WHITNEY ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- Th MAILING DATE of this communication app ars on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *171-192* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *171-192* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicant's arguments with regard to the priority were found persuasive. Therefore, this action will be non-final since it replaces the Tsien PCT with the Tsien patent (U.S. Patent 5,741,657), which is a 102(e) reference with regard to the September 1996 priority date. The Tsien patent has a 1995 102(e) date.

Claim Rejections - 35 USC § 112

2. The rejection of claims 171-177 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 171-192 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forrester et al (Proc. Natl. Acad. Sci. (February 1996) 93:1677-1682) in view of Tsien et al (U.S. Patent 5,741,657) and further in view of Hicks et al (Meth. Enzymol. (1995) 254:263-275).

Forrester teaches a plurality of eukaryotic clonal cells (see abstract), wherein each clonal cell comprises a distinct fusion RNA of a cellular RNA transcript and a B-galactosidase polynucleotide encoding a B-galactosidase, stating "Integration of PT1-ATG into the intron of an active gene can generate a fusion transcript between lacZ and an endogenous trapped gene" (see page 1677, column 2) and,

Wherein said clonal cells exhibit as much as a 12.4 fold induction in B-galactosidase expression in response to the induction of expression of said target in said clonal cells (See page 1678, table 1) in response to exposure of said clonal cells to a ligand for said target (see page 1677, column 2),

Wherein said clonal cells were selected from a population of cells transfected with the PT1-ATG vector and wherein said vector lacks a promoter to express said B-galactosidase (See page 1677, column 2).

With regard to claim 172 and 181, Forrester further teaches clonal cells under the control of the retinoic acid response element (see page 1678, table 1).

With regard to claims 173-176, 179, 180, 182 and 183, Forrester teaches the use of 24 well plates (a two dimensional array) (see page 1677, column 2). Forrester teaches screening of 3,600 ES (embryonic stem) cell colonies with 202 positive colonies picked and retested in the 24 well plates (see page 1678, column 1).

With regard to claims 177 and 184, Forrester teaches the use of ES cells which are emybryonic stem cells (see page 1677, column 2).

With regard to claims 187 and 190, Forrester teaches a 12.4 fold induction in B-galactosidase expression (See page 1678, table 1).

Forrester does not teach the use of B-lactamase in the place of B-galactosidase as the reporter. Also, it is unclear whether the vector of Forrester is a viral vector.

Tsien teaches the use of B-lactamase in the place of B-galactosidase (see column 3, lines 34-45). Tsien further teaches the limitation of claims 185 and 188 regarding membrane permeant substrates (see claim 10).

Hicks teaches the use of retroviral gene trap vectors (see page 267, page 268, figure 2 and entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to substitute the use the B-lactamase enzyme of Tsien for B-galactosidase since Tsien teaches "B-lactamases are nearly optimal enzymes in respect to their almost diffusion controlled catalysis of B-lactam hydrolysis. Upon examination of the other properties of this class of enzymes, it was determined that they were suited to the task of an intracellular reporter enzyme. (see column 3, lines 34-39)." Tsien identifies advantages of the use of B-lactamase which include high efficiency of the enzyme (see column 3, lines 34-35), since the enzymes are nearly optimally diffusion controlled (see column 3, lines 34-35).

It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to use retroviral

vectors as taught by Hicks since Hicks states that relative to ordinary vectors "[R]etrovirus vectors are easier to use, especially for large scale mutagenesis, and the structure of the recombination products is more predictable (see page 267). An ordinary practitioner would have been motivated to modify the method of Forrester in view of Tsien to use retrovirus gene trap vectors since the method of Forrester is a large scale mutagenesis method screening 3,600 colonies and since Hicks expressly teaches that this would be easier using a retrovirus gene trap vector.

Response to Arguments

6. Applicant's arguments filed July 2, 2003 have been fully considered but they are not persuasive.

7. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation is provided in the rejection. The motivation to use the beta lactamase of Tsien in the place of the Beta galactosidase of Forrester is given by Tsien, who notes that Beta lactamase is a nearly perfect enzyme which is suited to be an intracellular reporter. As noted, an ordinary practitioner would have been motivated to use a nearly perfect enzyme in the panel of Forrester. With regard to the use of the retrovirus vector,

Hicks teaches the advantages of such vectors for the types of assays employed by Forrester.

8. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies such as the ability to screen without the need for a secondary screening system are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Even if these limitations were included, they would represent intended use recitations. As MPEP 2111.02 notes "Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art."

Applicant finally argues that the references are silent regarding permeabilization of cells for the beta lactamase construct. This is not correct. Tsien expressly teaches the membrane permeability of the compounds, and in fact, actually claims this element (see claim 10).

Therefore, the rejections as altered are maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634

September 4, 2003